Sent by: Geffry King

04/24/2006 04:46 PM

To NCIC HPV@EPA

cc

bcc

Subject Re: Response to EPA comments: p-toluenesulfonyl isocyanate

Office of Pollution Prevention and Docket
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04/24/2006 01:02 PM

To NCIC OPPT@EPA, Rtk Chem@EPA

cc Matt Barmasse <M.Barmasse@SNPE.COM>, Mark Townsend/DC/USEPA/US@EPA

Subject Response to EPA comments: p-toluenesulfonyl isocyanate

Attached please find ISOCHEM Inc.'s response to EPA comments on the test plan **and** robust summaries for PTSI (CAS No. 4083-64-l). We will update the test plan and robust summary documents following completion of the vapor pressure study with this material. If you have any questions please do not hesitate to contact me or Mr. Mathew Barmasse at M.Barmasse@SNPE.COM

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SN354 p-TosylNCO EPA Comments 012606ResponsesApril_2006.doc

EPA Comments on Chemical RTK HPV Challenge Submission: p-Toluenesulfonyl isocyanate (PTSI)

SUMMARY OF EPA COMMENTS

The sponsor, ISOCHEM, Inc., submitted a test plan and robust summaries to EPA for p-toluenesulfonyl isocyanate (PTSI, CAS No. 4083-64-I) dated June 12, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on July 21, 2004. Information on a proposed analog, p-toluene-sulfonamide (PTSA, CAS # 70-55-3), was also included.

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. Data were provided for the hydrolysis product, PTSA, to satisfy most of the SIDS endpoints for PTSI. Although this approach is reasonable the submitter needs to support this rationale with measured sulfonyl isocyanate hydrolysis half-life data to confirm and better define "rapid" hydrolysis. ISOCHEM Response: Disagree. A hydrolysis study will not be performed with PTSI due to safety reasons. PTSI reacts spontaneously and violently with water. Water should not be poured into a vessel containing PTSI. Reaction with water results in the production of C02, and reaction vessels must be vented to avoid pressure build up.

2. Phvsicochemical Properties. The submitter needs to provide additional vapor pressure data for the sponsored substance. ISOCHEM Response: Agree. A vapor pressure study will be conducted in accordance with OECD guideline 104.

3. Environmental Fate. The submitter needs to provide measured ready biodegradation data for PTSA and more information on stability in water. ISOCHEM Response: A ready biodegradation study for PTSA is available on the UNEP website. This information will be included in the robust summaries and test plan for PTSI.

4. Health Effects. EPA reserves judgement on adequacy of PTSA data pending the submission of measured hydrolysis rate data. Then the submitter needs to address deficiencies in the PTSA robust summaries. ISOCHEM Response: Disagree. A hydrolysis study will not be performed with PTSI due to safety reasons. PTSI reacts spontaneously and violently with water. PTSA study details available on the UNEP website will be added to the existing robust summaries.

5. Ecological Effects. EPA agrees that it is reasonable to use data for the hydrolysis product, PTSA. However, the submitter needs to add the available measured data to the submission. ISOCHEM Response: Noted

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE P-TOLUENESULFONYL ISOCYANATE CHALLENGE SUBMISSION

Anaioa Justification

The submitter states that PTSI will hydrolyze rapidly to the corresponding carbamic acid followed by rapid decomposition to carbon dioxide and PTSA. The submitter proposes using data for PTSA to satisfy the SIDS endpoints for PTSI.

EPA considers this rationale generally reasonable. However, particularly for health effects evaluation, the submitter needs to support the approach by providing a measured hydrolysis half-life for PTSI or by submitting corresponding data for an appropriate analog(s) (see Environmental Fate section below).

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for melting point, boiling point, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program. ISOCHEM Response: Noted

Vapor pressure. The vapor pressure value provided by the submitter is not adequate for the purposes of the HPV Challenge Program. The submitter provided a single measured value of 1 mm Hg at 100 _C for PTSI. According to the HPV Challenge guidance, vapor pressure needs to be reported at 25 _C. Although extrapolated values from a series of measurements at elevated temperatures are acceptable in lieu of a measurement at 25 _C, a single measured high-temperature value is not adequate to address this endpoint. Therefore, the submitter needs to provide a measured vapor pressure value at 25 _C following OECD TG 104, or extrapolate a value from a series of measurements at elevated temperatures. ISOCHEM Response: Agree, A vapor pressure study will be conducted in accordance with OECD guideline 104.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for photodegradation and fugacity are adequate for the purposes of the HPV Challenge Program. ISOCHEM Response: Noted

Stability in water. The submitter stated that PTSI hydrolyzes rapidly to the corresponding carbamic acid followed by rapid decomposition forming carbon dioxide and PTSA. This assertion is reasonable. However, the submitter needs to support this rationale by providing a measured hydrolysis half-life for PTSI or by providing corresponding data for one or more analogous sulfonyl isocyanates, with technical discussion as appropriate. ISOCHEM Response: Disagree. A hydrolysis study will not be performed with PTSI due to safety reasons. PTSI reacts spontaneously and violently with water.
Biodegradation. The submitted data are not adequate for the purposes of the HPV Challenge Program because the test method used by the submitter relies on a single type of bacteria as inoculum (*Pseudomonas* sp.). The submitter needs to provide measured ready biodegradation data for PTSA, the hydrolysis product of PTSI, following OECD TG 301. ISOCHEM Response: A ready biodegradation study for PTSA is available on the UNEP website. This information will be included in the robust summaries and test plan for PTSI.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

With the exception of an acute toxicity value for PTSI, data for PTSA were submitted for the other health effects endpoints. The submitted PTSI data for acute toxicity are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the PTSA data for genetic, repeated-dose, reproductive and developmental toxicity until the hydrolysis issue is clarified (see above). When that occurs, the submitter will need to address deficiencies in the robust summaries because several important details are missing from the robust summaries for the screening test for repeated-dose/reproductive/

developmental toxicity (OECD TG 422), such as histopathology and information on parameters for assessing developmental toxicity. The submitter needs to consult the HPV guidance document for preparing robust summaries. ISOCHEM Response: Study details available on the UNEP website will be added to the existing robust summaries.

Ecological Effects (fish. invertebrates, and algae)

The submitter provided estimated data on PTSA for all endpoints. Although EPA agrees that it is reasonable to use data for the hydrolysis product PTSA, the submitter needs to include the measured PTSA data available on the UNEP website (http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html rather than the estimated values. Because the published OECD data for these effects predate the current data summary standards, the summaries need to be made robust for the purposes of the HPV Challenge Program. More study details may be available through the OECD SIDS contact for Japan:

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ISOCHEM Response: Agree. The PTSA data available on the UNEP website will be added to the robust summaries and Test Plan for PTSI.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The robust summary is missing the following information: species used, number of animals, route of exposure, doses used, organs evaluated at necropsy and the results of the evaluation. ISOCHEM Response: Additional information is not available for this study.

Repeated Dose/Developmental *and Reproductive* Effects. Information is needed as to the rationale for the selection of doses and use of vehicle. Specific information is needed on changes in body weight, food and water consumption, body weight at sacrifice, organ weight data, results and identification of tissues examined for histopathology, length of gestation, number of live births and post implantation loss, number of runts, number of implantations, corpora lutea (recommended), litter size and weights, time of death during the study and statistical treatment of the results. ISOCHEM Response: Agree. The PTSA data available on the UNEP website will be added to the robust summaries and Test Plan for PTSI.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.